

REMARKS

The present application is amended in a manner believed to place it in condition for allowance at the time of the next Official Action.

The present specification is amended. The "dialysis outer liquid inflow pipe" was inadvertently referred to as item "7" in the paragraph beginning on page 25, line 3. As the Figures 1 and 2 and the discussion on pages 14 and 15 clearly refer to the outer liquid inflow pipe as item "10", page 25 is amended to be consistent with the rest of the specification. No new matter is introduced in the specification.

Claims 19, 21-25 are amended.

Claim 20 is cancelled.

Claim 28 is new.

Support for the amended claims and new claim may be found generally throughout the specification, e.g., page 21, lines 3-22, Example 1, Figures 1, 2, and 4.

Claims 19, 21-26 and 28 remain pending.

The Official Action objects to the drawings for not showing "the thin film on the quartz thin plate" and "the surface portion of the inner vessel covered with the membrane". This objection is respectfully traversed.

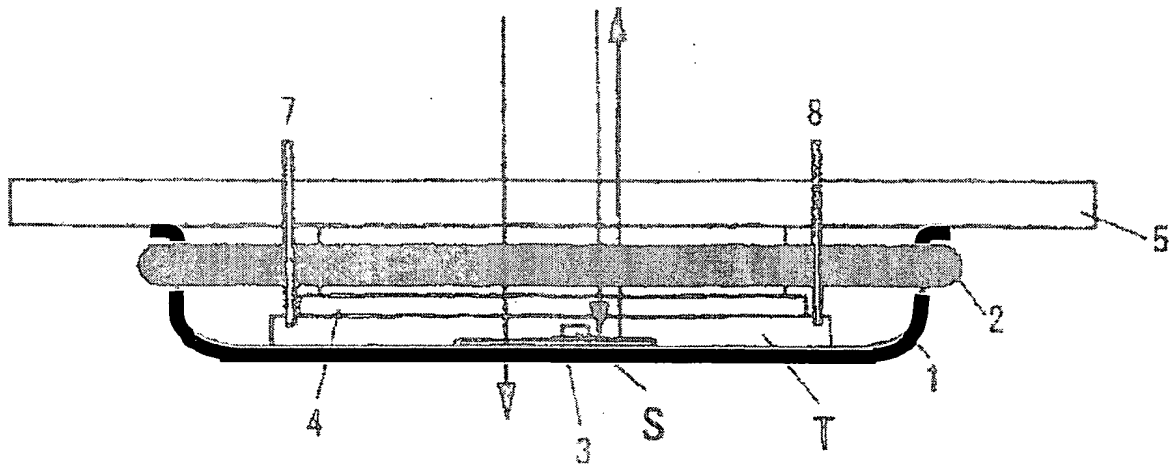
The "thin film on the quartz thin plate" is shown in Figures 1 and 3. At page 15, of the present specification, Figure 1 is described as including an item 3, which "denotes a quartz

thin plate having provided on a portion of the surface thereof a gold deposition layer (Au) that is a layer of a thin film for reflecting light (also referred as a light reflecting layer)". Additionally page 15 discloses "the arrow mark that is reversed at the portion of the light reflecting layer indicates a light path of a laser beam". Thus, the location of thin film is indicated by "3" and below the $\downarrow\uparrow$ of Figure 1, as well as "gold deposit portion" illustrated in Figure 3.

As to the "surface portion of the inner vessel covered with the membrane", the inner vessel is all that is shown in Figure 1, and the surface portion covered with the dialysis membrane is, thus, the portion covered by the membrane itself.

For example, on page 15, Figure 1 is described as showing "an inner vessel that contains the protein crystal and protein solution in a dialysis cell, illustrating the state that the protein crystal (S) to be measured is contained together with the protein solution (T)", "1 denotes a dialysis membrane", "2 denotes an elastic O-ring for fixing the dialysis membrane to a dialysis cell", and "7 and 8 denote an inflow pipe and an outflow pipe for the protein solution as means for flowing the protein solution having desired concentrations into the inner vessel". On page 14, it is noted that "[t]o fix the dialysis membrane to the inner vessel, an elastic O-ring is preferably used." Moreover, Example 1 describes, e.g., in the third paragraph of page 24, the plate, i.e., item 3, is placed in the inner vessel.

For illustration purposes, Figure 1 is provided below with the membrane represented by a dark bold line in contrast to the inner vessel depicted in Figure 1.



Therefore, the drawings do show the claimed features, and withdrawal of the objection is respectfully requested.

Claims 19-26 are rejected under 35 U.S.C. 112, second paragraph as being unclear. This rejection is respectfully traversed.

Specifically the claims are rejected for the means plus function language. The claims are amended in a manner that is clear.

As to "controlling a concentration of the protein in the protein solution", this may be accomplished by switching between a diluent and protein solution by varying a selector valve, as pointed out in the Official Action. This feature is now recited as a protein solution inlet source selector, which is

consistent with the present specification, e.g., the selector valve used to switch between protein solution and diluent as discussed specifically in the second full paragraph of page 21.

As to "controlling a concentration of a precipitating agent", this may be accomplished, for example, via two liquid transfer pumps operating at different throughputs. See, e.g., Example 1 and the first paragraph of page 17. The recitation is now a precipitating agent inlet concentration control element.

As to the "means for measuring a concentration of the precipitating agent", this is not simply a pump. Rather the precipitating agent concentration measurement device includes, for a salt solution, an electroconductivity meter, for determining the salt concentration from the outer vessel discharge. For a PEG based solution, the element includes a pump to control adding a buffer solution in an appropriate amount to a high concentration PEG solution to compare the resulting diluted PEG solution to the PEG solution of the outer vessel discharge. See, e.g, the paragraph bridging claims 19 and 20 and the first full paragraph of page 20.

As to claim 20, this claim is cancelled, and the features are recited in claim 19. Claim 19 is believed to be definite.

As to claim 22, claim 19 recites a "quartz thin plate" and "thin film". Thus, claim 22 no longer lacks antecedent basis.

As to claim 23 and 24, these claims now recite the outer vessel comprises the precipitating agent inflow element and the inner vessel comprises the protein solution inflow element, respectively. This is consistent with the description given in the descriptions of Figure 1 on page 15 and the description of Figure 2 on page 16, and the first full paragraph on page 17. Accordingly, the claims are definite.

As to claim 25, the "such as" expression is removed from the claim. Thus, the claim is now definite.

Therefore, withdrawal of the indefiniteness rejection is respectfully requested.

Claims 19 and 21-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over SHIRAISHI et al. US 5,362,325 (SHIRAISHI) in view of HARVEY US 4,717,824 (HARVEY). This rejection is respectfully traversed.

SHIRAISHI discloses an apparatus for growing crystals comprising a dialysis membrane, which can be applied to proteins. The apparatus comprises dialysis chamber 4 (container), which includes dialysis membrane 11, inner dialysis chamber 4a, outer chamber 4b, syringes 1a for introducing precipitating agents, and tubes 51, 42 as inflow elements. However, SHIRAISHI fails to disclose or suggest the invention as now claimed in independent claims 19 and 28.

For example, SHIRAISHI differs in that valve mechanism

29 is not an proteins solution inflow source selector, i.e., as it merely is used to open the outlet of one source, and cannot switch repeatedly between sources so as to control the concentration of the protein solution as recited in independent claims 19 and 28. Moreover, SHIRAISHI fails to disclose or suggest a quartz thin plate for the dialysis cell as recited in claims 19 and 28. Further, CCD camera 41 (Figure 7) is used only for observing the growth of crystals.

With respect to claim 28 in particular, each dialysis chamber of SHIRAISHI is limited to a single flexible tube 51 for introducing both protein solution and precipitating agent into the dialysis chamber, not a separate inflow element to a inner vessel and another inflow element to an outer vessel as recited in 28. The embodiment of SHIRAISHI that include two inlets or two inflow elements, i.e., Figures 14 and 15, is directed to vapor diffusion using a sponge, not a dialysis chamber with a dialysis membrane. See, e.g., column 11, lines 33-67.

HARVEY discloses a spectrophotometer with a Michelson interferometer for chemical analysis of a material in Figure 4. HARVEY fails to disclose or suggest that the spectrophotometer can be used in combination with an apparatus for growing protein crystals.

The position of the Official Action is that the claimed invention is obvious only because of the simple accumulation of the components of SHIRAISHI and HARVEY.

However, the combination fails to teach all of the features of the claimed invention, such as a protein solution/outer vessel inlet selector in claims 19 and 28, a dialysis cell as presently recited in claim 19, and separate inflow element or input for both protein solution and precipitating agent into a dialysis cell having a dialysis membrane as recited in claim 28. Thus, the proposed combination cannot render obvious independent claims 19 and 28, and dependent claims 20-26.

Therefore, withdrawal of the rejection is respectfully requested.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over SHIRAIISHI in view of HARVEY, further in view of WAGNER et al. US 2002/0115225 A1 (WAGNER). This rejection is respectfully traversed.

WAGNER discloses metal coated quartz substrates, where the metal coating enhances the optical characteristics of the substrates. However, WAGNER fails to disclose or suggest a dialysis cell and applying a metal coating to a substrate of a dialysis cell.

Even if one were to combine the teachings of WAGNER with SHIRAIISHI in view of HARVEY, WAGNER cannot remedy the deficiencies of the combination of SHIRAIISHI in view of HARVEY for reference purposes. As the combination fails to teach a protein solution/outer vessel inlet selector in claims 19 and 28,

a dialysis cell as presently recited in claim 19, and separate inflow element or input for both protein solution and precipitating agent into a dialysis cell having a dialysis membrane as recited in claim 28. Thus, the proposed combination cannot render obvious independent claims 19 and 28, and dependent claims 21-26.

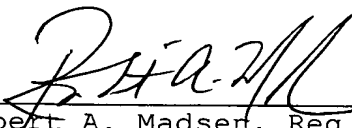
Therefore, withdrawal of the rejection is respectfully requested.

In view of the amendment to the claims and the foregoing remarks, applicants believe that the present application is in condition for allowance at the time of the next Official Action. Allowance and passage to issue on that basis is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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